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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,740	12/04/2006	Robert Hofmeister	028622-0148	5289

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
02/01/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,740	HOFMEISTER ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,13,15-17,19-26,32-35 and 37-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-7,9,13,15-17,19-26,32,33 and 41* is/are allowed.

6)☒ Claim(s) *34,35 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

1. Claims 20, 22, 24, 26, and 37 have been amended.

Claims 8, 10-12, 14, 18, 27-31, and 36 have been cancelled.

2. Claims 1-7, 9, 13, 15-17, 19-26, 32-35, and 37-41 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

Rejections Withdrawn

4. The rejection of claim 37 under 35 U.S.C. 112, second paragraph, as lacking antecedent basis is withdrawn in view of applicant's amendment to the claim.

5. The rejection of claims 20, 22, 24, and 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment to the claims.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 34, 35, and 37-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a nucleic acid sequence encoding the binding construct of claim 1 or comprising a vector or host cell comprising said nucleic acid sequence, does not reasonably provide enablement for a pharmaceutical composition comprising a nucleic acid sequence encoding the binding construct of claim 1 or comprising a vector or host cell comprising said nucleic acid sequence or for a method of treating a disease by administering the nucleic acid, vector, or host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to a pharmaceutical composition comprising a nucleic acid sequence that encodes a specific binding construct of claim 1, and a vector and host cell that comprise the nucleic acid sequence that encodes the binding construct of claim 1. The pharmaceutical composition is intended use by administering the composition

for therapeutic purposes. The claims are also drawn to a method of treatment by administering a nucleic acid, vector or host cell comprising the binding construct of claim 1.

As instantly recited, the claimed invention reads on broad genera of gene therapy (i.e. administration of nucleic acid or host cell), and gene therapy is generally not enabling due to problems with, inter alia, targeting and expression of transgenes at therapeutically effective level by vectors.

The specification fails to provide an enabling disclosure for the claimed invention because the specification fails to provide sufficient guidance as to (i) how an artisan of skill would have practiced the claimed method in treating any disease by administering via any route and expressing any nucleic acid or host, (ii) the claimed method would have resulted in expressing protein in amount sufficient to treat any subject having any disease.

While progress has been made in recent years for in vivo gene transfer, vector targeting in vivo to be desired organs continued to be unpredictable and inefficient. For example, numerous factors complicate the gene delivery art that could not have been overcome by routine experimentation. These include, the fate of DNA vector itself, volume of distribution, rate of clearance in tissue, the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of RNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory

fate, once produced. These factors differ significantly based on the vector used and the protein being produced (Goodman & Gilman's The Pharmacological basis of Therapeutics, McGraw-Hill, New York, NY. 1996. pages 77-101).

Next, the state of the prior art effectively summarized by the references of Verma and Somia (Nature, 1997. Vol. 389, pages 239-242) and Pfeifer and Verma (Annual Review of Genomics and Human Genetics, 2001. Vol. 2, pages 177-211) describes progress made in developing new vectors and also suggest vector targeting in vivo to be unpredictable and inefficient. Verma, et al., reviews various vectors known in the art for use in gene therapy and problems associated with each implying that at the time of claimed invention resolution to vector targeting had not been achieved in the art (Verma, et al., 1997; Pfeifer, et al., 2001; entire article). They highlight some advantages of using retroviral and adeno- associated viral vector in gene therapy but also acknowledge a greater level of skepticism in using these vectors in humans (Pfeifer, et al., 2001; abstract). It is noted by the authors that more efficient and safe vectors are required to deliver gene to the target cell for therapeutic effective level of gene expression (Pfeifer, et al. 2001; page 201).

The prior art on treating any subject having cancer by gene therapy was unpredictable. For instance, Vile, et al. (Gene Therapy, 2000, Vol. 7 pages 2-8) describe the unpredictability of gene delivery in the treatment of cancer and state, "Gene therapy for the treatment of cancer was initiated with high levels of optimism and enthusiasm. Recently, this perception has had to be tempered by the realization that efficiency and accuracy of gene delivery remain the most significant barriers to its

success. So far, there has been a disappointing inability to reach target cells with sufficient efficacy to generate high enough levels of direct killing and this has necessitated the invocation of bystander effects in order for any potential strategy to be convincing" (abstract).

Although human tumor xenografts implanted subcutaneously (sc) into nude mice as a predictive indicator of probable clinical activity has been validated for cytotoxic effects, Kelland, et al. (European Journal of Cancer, 2004. Vol. 40, pages 827-836) list several variables that impact on outcome; viz, site of implantation, growth properties of the xenograft and size when treatment is initiated, agent formulation, scheduling, route of administration and dose and the selected endpoint for assessing activity. Furthermore, Kelland emphasize that this model is valuable in preclinical cancer drug development, especially when such studies give due consideration to the above variables and are based on sound mechanistic and pharmacological principles (abstract). The specification also does not provide any guidance as to how studies in animal model can be extrapolated to human situations. In addition, prior art at the time of filing of this application as described before did not provide any convincing guidance in this regard either. Because the art, as shown above, does not disclose how the claimed vectors or hosts would be effective in any subject, the Artisan could not predict, in the absence of evidence to the contrary, that such applications as Applicant claims would be efficacious in therapeutic treatment. An artisan would have to carry out extensive experimentation to make use of the invention, and such experimentation would have been undue because of the art of gene therapy and gene delivery in vivo is

unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.

This suggests that undue experimentation would be required to practice the invention as broadly claimed. Given the above and given the absence of evidence in an in vitro or in vivo model drawn to the treatment of a disease by administering a nucleic acid or host, one of skill in the art would not believe it more likely than not that one of skill in the art could practice the claimed invention without undue experimentation.

Conclusion

8. Claims 1-7, 9, 13, 15-17, 19-26, 32, 33, and 41 appear to be in condition for allowance.

Claims 34, 35, and 37-40 are rejected.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
January 26, 2011

/Anne M. Gussow/
Primary Examiner, Art Unit 1643